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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,006	09/14/2005	Patrick Irving Eacho	X-13055	1872

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EXAMINER	
STOCKTON, LAURA LYNNE	
ART UNIT	**PAPER NUMBER**
1626	

NOTIFICATION DATE	DELIVERY MODE
10/16/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/550,006	EACHO ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-10,12,16 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6-10,12,16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 4, 6-10, 12, 16 and 18 are pending in the application.

Rejections made in the previous Office Action that do not appear below have been overcome by Applicant's amendments to the claims. Therefore, arguments pertaining to these rejections will not be addressed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6, 9, 10, 12, 16 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. No support is found in the instant specification or the originally filed claims for R_1 representing allyl in claim 1 and claim 3. Applicant did not state where support could be found for this amendment to the claims. Applicant should specifically point out the support for any amendments. See M.P.E.P. §§ 714.02 and 2163.06. Therefore, the claims lack written description as such.

Claims 10, 12 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating hypercholesterolemia, hyperlipidemia or atherosclerosis, does not reasonably provide enablement for treating all diseases which are affected by hepatic lipase. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

Applicant is claiming a method of inhibiting hepatic lipase and a composition for the treatment of the effects of elevated hepatic lipase comprising a compound of formula (I). From the reading of the specification, it appears that Applicant is asserting that the instant claimed compounds would be useful for the treatment of numerous diseases and disorders. See page 4 of the instant specification.

The state of the prior art and the predictability or lack thereof in the art

The state of the art is that the treatment of diabetes remains highly unpredictable. Colagiuri et al. {American Journal of Public Health, September 2006, Vol. 96, No. 9, pages 1562-1569} state "Type 2 diabetes is a complex metabolic disorder triggered by lifestyle factors superimposed on a genetic predisposition." Colagiuri et al. also state "Although we recognize the benefits of science, surgery, and service delivery in relation to certain aspects of chronic disease

prevention, it is clear that, either independently or in concert, none can achieve the broad scale changes required to prevent diabetes and obesity on a population basis."

According to Bruno et al. {Expert Opinion Emerging Drugs, (2005), 10(4), pages 747-771}, diabetes mellitus is a major health problem that affects over 170 million people worldwide. Park {Diabetes Research and Clinical Practice 66S (2004), S33-S35} states current methods of treating diabetes is inadequate and that current strategies to prevent type 2 diabetes mellitus are based on efforts to reduce insulin resistance and to preserve or increase pancreatic beta cell function in high risk individuals. Park also states, "It appears that multiple genes with weak effect are involved in the development of type 2 diabetes mellitus which makes searching diabetogenic genes more complicated." Further, Choi et al. {Journal of Lipid Research, Volume 43, 2002, pages 1763-1769} indicate that there is some

suggestion that endothelial lipase plays a role in the development of atherosclerosis. Choi et al. also state, "However, there is only limited amount of information available about this enzyme" and that more studies are needed. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

That a single class of compounds can be used to treat all of the diseases and disorders embraced by the claims is an incredible finding for which Applicant has not provided persuasive supporting evidence.

The quantity of experimentation needed

The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities for each of the diseases instantly claimed

in the composition. The quantity of experimentation needed would be undue when faced with the lack of testing, and when faced with the unpredictability of the pharmaceutical art. Thus, factors such as "sufficient working examples", "the level of skill in the art" and predictability, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

The level of the skill in the art

Even though the level of skill in the pharmaceutical art is very high, based on the unpredictable nature of the invention and state of the prior art, one skilled in the art could not use the claimed invention without undue experimentation.

Response to Arguments

Applicant's arguments filed August 3, 2007 have been fully considered but they are not persuasive. Applicant argues that the present application provides

sufficient enablement because of the assay disclosed in the instant specification. In response, the instant specification fails to demonstrate or show a nexus between being able to effect elevated hepatic lipase activity and treating each and every disease embraced by the broad language of the instant claims. The rejection is deemed proper and therefore, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-10 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is confusing since the claim begins with "selected from…"; ends with "and"; and there is no period at the end of the claim.

Claim 8 does not conform to M.P.E.P. 608.01(m) since each claim must end with a period thereby establishing that no other subject matter is missing from the claim.

In claim 9, a space is needed in "according to claim 1".

In claim 10, the purpose for "inhibiting hepatic lipase and/or endothelial lipase activity" has not been stated in the claim {e.g., to treat what?}.

In claim 18, it is unclear how a therapeutically effective amount of a compound of formula I is used and who or what it is used on.

Response to Arguments

Applicant's arguments filed August 3, 2007 have been fully considered but they are not persuasive.

Applicant argues that the claims have been amended to correct the problems. However, in the case of claims 7 and 8, Applicant has introduced new problems. Applicant argues that in regard to claim 10, the effect of the method does not need to be recited in the claim. In response, so that the metes and bounds of the claim can be ascertained, the effect of the method does need to be recited in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 6-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi et

al. {JP 48-029134}. An English translation of the Japanese document has been supplied with this Office Action and will be referred to hereinafter.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicant claims benzisothiazolone compounds. Takahashi et al. (page 1; and especially the second compound listed on page 3) teach benzisothiazolone compounds that are structurally similar to the instant claimed compounds.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the compounds of the prior art and the compounds instantly claimed is that the instant claimed compounds is that of hydrogen versus methyl of the phenyl ring of the benzyl group {i.e., instant R_1 is an alkyl substituted benzyl}

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

It is well established that the substitution of a lower alkyl for a hydrogen atom {i.e., a homolog} on a known compound is not a patentable modification absent unexpected or unobvious results. *In re Lincoln*, 53 U.S.P.Q. 40 (C.C.P.A. 1942), *In re Druey*, 138 USPQ 39 (C.C.P.A. 1963) and *In re Lohr*, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e., a fungicide).

One skilled in the art would thus be motivated to prepare homologs of the compounds taught in the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful as fungicides. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Response to Arguments

Applicant's arguments filed August 3, 2007 have been fully considered but they are not persuasive. Applicant argues that: (1) structural similarity between the prior art compounds and the claimed compounds by itself is not suffice to support a *prima facia* rejection; and (2) Takahashi et al. teach fungicidal compounds.

In response, there is no requirement that the prior art must suggest that the claimed product will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. *In re Dillon*, 16 U.S.P.Q. 2d 1897, 1904 (Fed. Cir. 1990). The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Conclusion

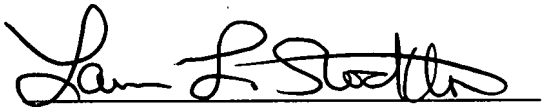
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.



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October 10, 2007